

Hot flushes in breast cancer patients

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Abstract

Objectives: A literature search was conducted to gather information concerning the pathophysiologic mechanisms leading to hot flushes, their prevalence and severity in breast cancer patients, their influence on quality of life, and the best therapeutic option.

Methods: Relevant studies in English were selected from Medline.

Results and conclusion: Pathophysiologic mechanisms leading to hot flushes are poorly understood. Estrogen withdrawal is considered to have a central role. Also, serotonin and norepinephrine seem to be involved in hot flush induction. Menopause induced by chemotherapy or

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ovarian ablation, is accompanied by an abrupt decrease in estrogen level, causing vasomotor symptoms. Hot flushes are also a side effect of tamoxifen and aromatase inhibitors. Quality of life in breast cancer patients may be negatively influenced by hot flushes, and therefore, adequate treatment is important. Currently, of the several non-hormonal options, the selective serotonin-reuptake inhibitor (SSRI) venlafaxine is the most effective in breast cancer patients. However, studies on interaction between SSRIs and tamoxifen may influence future recommendations. © 2005 Elsevier Ireland Ltd. All rights reserved.

Keywords: Hot flushes; Breast cancer; Menopause; Clonidine; SSRI

1. Introduction

Hot flushes are common in post- and perimenopausal women. In women treated for breast cancer, the prevalence of vasomotor symptoms is higher than in healthy women, and hot flushes often occur at a younger age. As a growing number of women receive adjuvant chemotherapy and/or endocrine therapy for their breast cancer, and as more women survive breast cancer nowadays, treatment of hot flushes in these patients becomes increasingly important. Treatment options, however, are limited.

In healthy women with hot flushes, hormonal therapy with estrogens, either combined with or without progestagens, is very effective in reducing bothersome hot flushes, but has been under fire lately. This is due to small, but significant, increases in the risks of coronary events, stroke, pulmonary embolism and breast cancer associated with hormone replacement therapy in healthy, postmenopausal women [1,2]. Especially combinations of estrogen and progestagen are associated with a higher risk of breast cancer [1–3]. Because of the concerns about the influence of hormones on breast cancer, estrogens and estrogen–progestagen combinations are regarded to be contraindicated in breast cancer patients. Safe alternatives are needed to adequately treat hot flushes in these women. Over the last decades new drugs for alleviating vasomotor symptoms have emerged with marked differences in efficacy and side effects.

Apart from the therapeutic considerations, there is still much to be learnt about the mechanisms responsible for the development of hot flushes and the associated risk factors. Furthermore, despite the prevalence of hot flushes, little is known about the their influence on quality of life.

2. Study objectives

The purpose of this paper is fourfold. The first objective is to describe the pathophysiologic mechanisms leading to hot flushes, the second to give an explanation for the prevalence of more frequent and more severe hot flushes in patients treated for breast cancer, the third objective is to describe the influence of hot flushes on quality of life in these patients, and the last is to describe the currently most effective, best tolerated, and also safe, drug options for the treatment of hot flushes in women with a history of breast cancer.

A literature search was conducted to find appropriate data with respect to these objectives. In order to provide the nec-

essary background information, literature was additionally searched for data about menopause and vasomotor symptoms in healthy women.

3. Data sources and study selection

Relevant studies were identified by using the Medline database. Literature from the period 1977 to 2005 and written in English was searched with the search terms: hot flushes, hot flashes (used in American literature), menopause, pathophysiology, quality of life, breast cancer, chemotherapy, endocrine therapy, tamoxifen, ovarian ablation, LHRH analogues, hot flush therapy, hormonal replacement therapy, estrogen, progestagen, clonidine, SSRI, venlafaxine, fluoxetine, paroxetine, Vitamin E, phytoestrogen, gabapentin, Bellerger, black cohosh. These search terms were used in varying combinations to identify the most suitable literature for this paper. Also, reference lists of selected papers were used to find articles that did not appear in the primary search.

Studies were selected if they were original papers or reviews. Large randomized, double-blind, placebo-controlled trials were preferable to small, non-placebo-controlled trials. However, the use of small, non-controlled studies was not always avoidable, due to the limited amount of literature with respect to certain subjects. For example, for some drugs no large comparative trials have (yet) been conducted. Case reports were excluded. Studies were used if they were relevant in serving the objectives of this paper.

4. Results

4.1. Menopause

Hot flushes occur as part of the symptom complex associated with menopause. Menopause is being defined as the permanent cessation of menstruation due to ovarian failure and marks the end of a woman's reproductive life. Postmenopause dates from the menopause, but can only be determined retrospectively, as a period of 12 months of amenorrhea has occurred. Women in whom the ovaries have been removed are considered postmenopausal as well. Perimenopause corresponds to the period of transition from regular menstruation to its cessation. Perimenopausal status in women can be further defined as being late perimenopausal: menstruation has occurred in the past 12 months, but not in the last 3 months;

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